METHOD OF SEALING A CARTRIDGE OR OTHER MEDICAL CONTAINER WITH A PLASTIC CLOSURE

RELATED APPLICATIONS

[0001] This application is a continuation in part application of Serial No. 09\732,538 filed December 8, 2000 and Serial No. 09\421,657 filed October 20, 1999, which applications are continuation-in-part applications of Serial No. 09\168,502 filed October 8, 1998, which claims priority under 35 U.S.C. Section 119e to U.S. Provisional Application Serial No. 60\082,372, filed April 20, 1998.

FIELD OF THE INVENTION

[0002] This invention relates to an improved method of sealing a medical cartridge or other medical container containing a medicament, drug or vaccine, which eliminates the problems associated with malleable metal caps or collars, such as aluminum. The method of this invention may be used to seal a cartridge having an elastomeric stopper with a polymeric cap or closure.

BACKGROUND OF THE INVENTION

[0003] It is conventional to store medicaments, drugs or vaccines in a sealed cartridge or other container for later use. Such medicaments, drugs or vaccines may be in liquid or dry or powdered form to increase the shelf life of the drugs and reduce inventory space. Such dry or powdered medicaments, drugs or vaccines are generally stored in a sealed cartridge and reconstituted in liquid form for administration to a patient by adding a diluent or solvent. A conventional medical cartridge for storing medicaments generally includes an open end, a radial rim portion surrounding the open end and a reduced diameter neck portion adjacent the rim portion. The cartridge is conventionally sealed with an elastomeric stopper or septum which

generally includes a central portion overlying the open end of the cartridge and a planar radial rim portion which overlies the cartridge rim. The stopper is normally secured to the cartridge with a thin malleable metal cap, such as aluminum. The aluminum cap includes a tubular portion which surrounds the rim portions of the stopper and cartridge, an inwardly projecting annular portion which overlies the rim portion of the stopper and a distal end portion which is crimped radially into the neck of the cartridge beneath the rim portion. Because aluminum is malleable, the collar accommodates the buildup of tolerances of the dimensions of the stopper and rim. The dimensions and tolerances of standard cartridges and stoppers are set by the International Standards Organization (ISO).

[0004] The radial portion of the aluminum cap which overlies the stopper rim portion may be closed, in which case the aluminum cap is removed by "peeling" the aluminum cap from the cartridge. A pre-slit tab located in the middle area may be provided which overlies the cartridge rim, permitting the cap to be torn from the top and peeled from the cartridge prior to use. This closed embodiment of an aluminum cap has several disadvantages. First, the tearing of the metal cap creates sharp edges which may cut or damage sterile gloves and cut the person administering the drug, thereby exposing both the healthcare worker and the patient to disease and contamination of the drug. Second, the tearing of the aluminum cap generates metal particles which may also contaminate the drug, medicament or vaccine. The dangers associated with the tearing of an aluminum cap has been solved in part by adding a "flip-off" plastic cap. In one such embodiment, the aluminum collar includes a central opening and a shallow plastic cup-shaped cap is received over the aluminum collar having a central projecting riveting portion which is received and secured in the central opening of the aluminum collar. The plastic cap is then removed by forcing the flip-off cap away from the aluminum collar, which tears an annular serrated portion surrounding the central opening and exposes an opening in the collar for receipt of a needle cannula or the like. This embodiment reduces but does not eliminate the possibility

of tearing the sterile gloves of the healthcare worker. More importantly, however, aluminum dust is still created during crimping of the aluminum cap which may contaminate the medicament, drug or vaccine contained in the cartridge. It is also important to note that metallic dust is also created simply by forming and affixing the aluminum cap or collar to the cartridge because aluminum dust is created in forming the aluminum collar, crimping of the collar and removal.

[0005] Various types of medical cartridges are now available for delivery of a medicament, drug or vaccine. A medical cartridge includes a tubular barrel portion, typically formed of glass, having open proximal and distal ends, wherein the proximal end includes a radial rim portion and a reduced diameter neck portion adjacent the rim portion. The proximal open end of the cartridge is sealed with an elastomeric stopper having a central portion overlying the open proximal end of the cartridge and a rim portion overlying the rim portion of the cartridge. The proximal open end of the cartridge is sealed with a malleable metal cap generally formed of aluminum including a tubular collar portion surrounding the rim portion of the cartridge which is crimped around the rim portion into the neck portion of the cartridge. The cap further includes a radial portion overlying the rim portion of the elastomeric stopper and the cap generally includes a central circular opening coaxially aligned with the opening through the proximal end of the cartridge. The cap is secured to the proximal end of the cartridge by resiliently compressing the radial portion of the cap against the rim portion of the elastomeric stopper and crimping the free end of the collar portion into the neck portion of the cartridge.

[0006] The open distal end of the cartridge is sealed with a stopper, generally formed of an elastomeric material, which serves as a plunger to propel the fluid through the proximal open end of the cartridge. The cartridge may be utilized in a delivery pen, for example, as disclosed in U.S. Patent No. 5,549,575 assigned to the assignee of the present application, the disclosure which is incorporated herein by reference. A delivery pen typically includes a needle assembly

received on the proximal end of the body portion having a needle cannula which pierces the elastomeric stopper or septum which seals the proximal end of the cartridge and the stopper in the distal end of the cartridge is then driven through the barrel portion to dispense a liquid medicament, drug or vaccine through the needle cannula during an injection. The medical cartridge may also include a third stopper centrally located within the barrel portion which, during injection, intermixes the substances contained in the barrel portion between the stoppers as discussed further below.

[0007] The need therefore remains for a method of sealing cartridges and other medical containers which may be utilized for sealing conventional medical cartridges, which assures sealing of the container and which achieves a good level of cleanliness, without metal particles or dust which may contaminate the medicament, drug or vaccine, and which does not expose the health care worker to sharp edges. The method of sealing a medical container of this invention solves these problems and permits sealing of medical containers in an aseptic environment.

SUMMARY OF THE INVENTION

[0008] As set forth above, the method of sealing a cartridge or other medical container with a plastic closure of this invention eliminates the problems associated with malleable metal or aluminum caps or collars, but which accommodates build-up of tolerances of the rim portion of the container and the elastomeric stopper, when used. The plastic or polymeric closure of this invention is relatively inexpensive to manufacture and use in the method of this invention. The method of this invention may be utilized to seal a conventional medical cartridge with a polymeric cap and for transferring fluids between the stoppers of a medical cartridge. As used herein, the term "closure" is generic to either a cap or collar.

[0009] As stated above, the method of sealing a container with a plastic closure of this invention may be utilized with a conventional cartridge or other medical container having an

open proximal end, a radial rim portion surrounding the proximal open end and a reduced diameter neck portion adjacent the rim portion. The method of sealing a medical cartridge or other container with a plastic closure of this invention includes forming a plastic closure from a polymer, preferably formed by injection molding, which is sufficiently malleable to permit radial deformation, yet sufficiently rigid to retain its shape following deformation and sufficiently resistant to creep to maintain a seal between the plastic closure and the cartridge rim following radial deformation. The plastic closure formed by the method of this invention includes a generally cylindrical tubular collar portion having an internal diameter generally equal to or preferably slightly greater than an outside diameter of the rim portion of the container and an integral radial rim portion preferably having a central opening. In the preferred method of this invention, the plastic closure is formed by injection molding a polymer alloy comprising a relatively malleable soft polymer and a relatively rigid polymer. The closure may be formed by co-injecting a polymer alloy which preferably includes a polycarbonate as the relatively rigid polymer.

[0010] The method of this invention then includes telescopically disposing the tubular portion of the closure over the rim portion of the container with the radial rim portion of the closure overlying the rim portion of the container and the generally cylindrical tubular portion surrounding the container rim having a free end surrounding the reduced diameter neck portion of the container. The tubular portion of the closure adjacent the free end is then incrementally deformed and rolled radially inwardly into the neck portion of the container beneath the rim portion and preferably against the rim portion adjacent the neck portion, permanently securing the closure on the container and sealing the container open end, wherein the free end of the plastic closure retains its shape beneath the radial rim portion following deformation and the polymer is sufficiently resistant to creep to permanently maintain the seal. In the preferred method of sealing a cartridge having medicament, drug or

vaccine therein, the cartridge is initially sealed with an elastomeric stopper having a planar rim portion which overlies the rim portion of the cartridge. The method of this invention then preferably includes compressing the radial rim portion of the plastic closure against the radial portion of the stopper to seal the plastic closure to the stopper and substantially simultaneously radially incrementally deforming and rolling the free end of the closure tubular portion into the reduced diameter neck portion of the cartridge as described above.

[0011] In the preferred method of sealing a container, such as a medical cartridge, with a plastic or polymeric closure of this invention, the cylindrical tubular portion of the closure is incrementally deformed radially and rolled into the neck portion of the container using a crimping tool or tools having inclined, chamfered or tapered surfaces and the cartridge or container and the crimping tool are relatively rotated and driven together to deform or incrementally roll the tubular portion of the closure both radially into the neck portion of the collar and axially against the adjacent rim portion of the container to permanently secure the closure on the container and seal the container. In one preferred embodiment of the method of this invention, the crimping tool includes a plurality of frustoconical chamfered surfaces which are rotated and driven against the tubular portion of the closure, incrementally rolling the collar into the neck portion of the cartridge as described. In this embodiment, the cartridge or container may be simultaneously rotated to incrementally crimp and seal the entire periphery of the rim portion. In another embodiment, the crimping tool includes an arcuate or circular stationary rail having an inclined or frustoconical chamfered surface and the method of crimping the closure includes simultaneously driving the cartridge and closure assembly against the rail and rotating the cartridge assembly to incrementally roll the free end of the tubular portion of the closure radially inwardly into the reduced diameter neck portion and axially against the adjacent rim portion of the cartridge as described. In either embodiment, the method is preferably a cold forming process dependent upon the material of

the polymeric closure, which as described as above is sufficiently malleable to permit radial deformation, yet sufficiently rigid to retain its shape following deformation and sufficiently resistant to creep to maintain the seal between the plastic closure and the cartridge following radial deformation.

[0012] In both preferred embodiments of cold forming by incrementally rolling the free end of the plastic closure into the reduced diameter neck portion of the cartridge or other container, the free end of the tubular collar portion is preferably gradually or incrementally deformed radially into the neck portion to assure permanent deformation, reduced creep and reduce damage to the closure, such as stress cracking or discoloration of a clear plastic closure. In the first embodiment of the method of this invention described above, the free end of the tubular closure is deformed incrementally by a series of rotating crimping tools, wherein the first tool has a relatively steep angle of inclination, such as 45 degrees. The angle of inclination of the next crimping tool is then reduced, etc. to the desired angle of the deformed lip, which may be, for example, 20 to 30 degrees. In the second embodiment of the method of this invention described above, the angle of inclination of the crimping surface of the rail is gradually and continuously reduced as the cartridge or other container is rolled or rotated along the rail gradually cold forming and rolling the free end of the closure into the cartridge neck thereby avoiding damage to the cartridge rim portion and the closure, including cracking and discoloration.

[0013] One important advantage of the method of sealing a cartridge or other medical container of this invention is that the container may be a conventional medical cartridge, as described above, having a conventional elastomeric stopper.

[0014] The method of sealing a transfer set on a cartridge or other medical container with a plastic closure of this invention then includes first assembling the stopper or stoppers on the medical cartridge. The closure is then assembled on the cartridge or other medical

container by telescopically receiving the tubular collar portion of the closure over the rim portion of the cartridge such that the tubular collar portion surrounds the rim portion of the cartridge and at least a portion of the reduced diameter neck portion. The method of this invention then includes incrementally rolling and radially deforming the free end of the tubular collar portion of the closure into the reduced diameter neck portion of the container and preferably against the adjacent radial rim portion, permanently securing the closure on the cartridge and sealing the cartridge as described above. That is, the tubular collar portion is preferably gradually or incrementally deformed or cold rolled as described above. In the most preferred embodiment of the method of sealing a cartridge of this invention, the radial portion of the closure is simultaneously compressed against the radial planar rim portion of the elastomeric stopper on the proximal open end of the cartridge as the tubular collar portion is incrementally crimped into the neck portion of the cartridge

[0015] As set forth above, the method of sealing a cartridge or other medical container with a plastic closure of this invention utilizes a polymer for the closure having the requisite physical properties to provide and maintain a seal between the plastic closure and the cartridge or other medical container and permanently secure the closure on the container. In the preferred embodiment, the plastic closure is formed of a polymer alloy or melt blend which includes a relatively tough soft malleable copolymer and a relatively rigid copolymer. In the most preferred embodiment, the composite polymer is a polymeric alloy of a relatively soft malleable copolymer and a relatively rigid polymer. The preferred rigid polymer is a polyamid or a polycarbonate and the preferred relatively soft copolymer may be selected from polyesters or polyolefins. The resultant polymer alloy or composite preferably has an elongation at yield between 5% and 10% and an elongation at break greater than 100% with a flectural modulus of greater than 1,900 MPa.

[0016] The method of this invention thus eliminates the problems and hazards associated with the use of a malleable metal closure or collar, such as aluminum, and plastic coated aluminum caps or collars while assuring sealing of the cartridge or other medical container or damage to the plastic closure or cartridge rim portion. In the most preferred embodiment of the method of this invention, the plastic closure or collar is formed by injection molding the plastic closure from a polymeric alloy or composite as described. A thermoplastic elastomer may also be co-injected with the polymer forming the closure to form a coating or film on the inside surface of the closure, which is integrally bonded to the polymer of the closure. As used herein, the terms "composite" and "alloy" are used in their broadest sense to include alloys or melt blends, composites and copolymers.

[0017] Other advantages and meritorious features of the method of sealing a cartridge or other medical container with a plastic closure or collar of this invention will be more fully understood from the following description of the preferred embodiments, the appended claims and the drawings, a brief description of which follows.

BRIEF DESCRIPTION OF THE DRAWINGS

[0018] Figure 1 is a partial side cross-sectional side view of a plastic closure secured to a medical cartridge in sealed relation formed by the method of this invention;

[0019] Figure 2 is an exploded side crosssectional view of the components of the assembly shown in Figure 1 illustrating the method of assembling the closure and stopper on the cartridge;

[0020] Figure 3 is a partially crosssectioned side view of the assembly shown in Figures 1 and 2 schematically illustrating one embodiment of the method of crimping the closure on the cartridge;

[0021] Figures 4 to 6 illustrate one preferred method of crimping a closure on the medical cartridge shown in Figures 1 and 3, wherein Figure 4 is a perspective top view;

[0022] Figure 5 is a partially crosssectioned side view of Figure 4 in the direction of view arrows 5-5; and

[0023] Figure 6 is an enlarged side partially cross-sectioned view of Figure 4 in the direction of view arrows 6-6;

[0024] Figures 7 to 10 illustrate an alternative method of sealing a cartridge, wherein Figure 7 is a top perspective view and Figures 8 to 10 are a side partially cross sectioned views in the direction of view arrows 8-8, 9-9 and 10-10, respectively;

[0025] Figure 11 is a side cross-sectioned view of an alternative embodiment of a cartridge sealed by the method of this invention.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

[0026] Figures 1 to 3 illustrate one preferred embodiment of the cartridge, stopper and closure assembly 20 sealed by the method of this invention. As set forth above, the method of this invention may be utilized to seal various containers and is particularly useful for sealing the proximal end of a medical cartridge 22 illustrated in Figures 1 to 3. The cartridge includes an open proximal end 24, an annular radially extending rim portion 26 and a reduced diameter neck portion 28 adjacent the rim portion. As shown, the neck portion 28 of the cartridge has a reduced diameter when compared to the rim portion 26 and the container portion 30 shown in Figure 6. Medical cartridges of this type are generally formed of glass but may also be formed of a sterilizable plastic. The open end 24 of the cartridge is typically closed with an elastomeric stopper 32 having a planar rim portion 36 which overlies the rim portion 26 of the cartridge as shown in Figure 1. The stopper is generally formed of a resilient elastomeric material such as synthetic or natural rubber. The central portion 38 of the stopper may be pierced with a

hypodermic needle, for example, to either withdraw fluid from the cartridge or add a solvent or diluent to the cartridge where the medicament, drug or vaccine in the cartridge is a dry or powdered material.

[0027] A preferred embodiment of the closure or cap 40 is shown in Figure 1 attached to a cartridge 22 and stopper 32 assembly, prior to assembly in Figure 2 and during assembly in Figure 3. This embodiment of the closure 40 includes a tubular collar portion 42 which surrounds the rim portion 26 of the cartridge and the planar rim portion 36 of the stopper. Where the external surface of the rim portion 26 of the cartridge is cylindrical, the tubular collar portion 42 of the closure will generally also be cylindrical. As shown in Figure 1 and described below, the free end 44 of the tubular collar portion 42 is incrementally deformed radially inwardly and rolled into the reduced diameter neck portion 28 and against the adjacent surface of the rim portion 26 of the cartridge, permanently securing the collar 40 on the cartridge and sealing the cartridge and avoiding damage to the polymeric closure and rim portion of the cartridge.. The preferred embodiment of the closure 40 also includes an integral radial proximal portion 46 which overlies the rim portions 26 and 36 of the cartridge and stopper, respectively. The radial portion 46 is preferably integrally molded with the tubular collar portion 42 of the closure. This embodiment of the closure 40 also includes a central opening 48 which overlies the central portion 38 of the stopper, preferably coaxially aligned with the central portion 38 of the stopper. The central opening 48 may however, be eliminated in certain applications of this invention where the polymeric closure is pierceable. As used herein, the terms proximal and distal are used solely for ease of description, wherein the term proximal refers to elements or portions of elements closest to the rim portion 36 of the stopper and distal refers to elements or portions of elements more remote from the rim portion of the cartridge. Further, the terms cap and collar are sometimes used herein interchangeably.

[0028] The closure 40 is then assembled on the cartridge 22 and stopper 32 as shown in Figure 2. In a typical application, a second stopper 50 is first inserted into the distal end 52 of the cartridge 22, after the cartridge is filled as shown in Figure 6. As set forth above, the plastic closure 40 of this invention may be used with various containers particularly including conventional medical cartridges as shown. Thus, in a typical application, the cartridge 22 may be filled with a medicament, vaccine or drug prior to or after securing the closure 40 on the proximal end of the cartridge. The tubular portion 42 of the closure 40 is then received over the rim portion 36 of the stopper and the rim portion 26 of the cartridge as shown in Figure 3 and describe below.

[0029] A method of crimping the closure or cap 40 on the cartridge 22 is schematically shown in Figure 3. The free end 44 of the tubular collar portion 42 of the closure is crimped or rolled on the cartridge by a crimping tool 58 having an inclined or tapered surface 60 which, in the disclosed embodiment, is frustoconical. The crimping tool 58 is rotated in one direction as shown by arrow 62 and, in this embodiment, the assembly of the closure 40 and cartridge 22 is rotated at the same speed in the opposite direction as shown by arrow 64 and thereby rolled into the neck 28 of the cartridge. The inclined frustoconical surface 60 is driven against the tubular portion 42 of the closure as shown by arrow 68 or vice versa, which deforms the free end 44 radially inwardly against the reduced diameter neck portion 28 and against the rounded edge 66 of the rim portion 26 adjacent the neck portion 28. The radial portion 46 of the closure is preferably simultaneously compressed against the planar radial rim portion 36 of the elastomeric stopper 32 to assure complete sealing of the cartridge. In the preferred method of sealing a medical container with a closure of this invention, the tubular portion 42 is incrementally deformed and rolled into the reduced diameter neck portion 28 by cold forming. That is, the crimping tool 58 is not heated to soften or partially melt the polymeric closure as would be required with certain polymers. Thus, as described below, the preferred polymer for the closure

is selected based upon its physical properties, as described above. In the most preferred embodiment of the method of sealing a cartridge or medical container with a closure of this invention, the tubular portion 42 of the closure is gradually or incrementally deformed and rolled into the reduced diameter neck portion 28 of the cartridge using a plurality of crimping tools having different degrees of inclination or pitch or the rim portion is deformed against a crimping tool having a gradual change of pitch as described below with regard to Figures 4 to 6 and 7 to 10 respectively.

[0030] The cartridge 22 is now ready for use. As will be understood by those skilled in this art, the cartridge may be filled with a medicament, drug or vaccine and used with a variety of delivery devices, such as the medicament delivery pen disclosed in the above referenced U.S. Patent No. 5,549,575. The stopper 50 is conventionally received in the distal end 52 of the cartridge 22, which is generally referred to as the barrel of the cartridge. A cartridge of this type may be utilized to deliver liquid medicaments, drugs or vaccines or used to reconstitute a dry or lyophilized medicament, drug or vaccine powder as discussed further in regard to Figures 10 and 11, below. The stopper 50 adjacent the distal end 52 of the cartridge serves as a plunger, which is driven through the cartridge barrel. A needle cannula (not shown) pierces the central portion 38 of the stopper 32 to deliver the medicament, drug or vaccine through the needle cannula as is well known in this art.

[0031] The polymer selected for the plastic cap or closure 40 and method of this invention can best be described by its required physical properties. The polymer must be sufficiently malleable to permit radial deformation or crimping, yet sufficiently rigid to retain its shape following deformation. The polymer must also be sufficiently resistant to creep to maintain the seal between the plastic collar portion and the container following radial deformation. It has been found that a polymer having an elongation at yield between 5% and 10% and an elongation at break greater than 100%, combined with a flexural modulus of greater than 1900 MPa has

superior performance. Where the plastic closure of this invention is utilized for sealing cartridges containing a medicament, vaccine or drug, the polymer should also be sterilizable and, in certain applications such as the plastic closure for a cartridge transfer set described below, the polymer is preferably relatively clear and maintains its clarity under the stress of deformation or crimping. It has been found that certain polymer alloys or composite polymers including melt blends or alloys and co-polymers having polymers of different malleability and rigidity are preferred in these applications. That is, the plastic closure used in the method of this invention is preferably formed of a polymer alloy, composite polymer or co-polymer including a relatively rigid polymer and a tough relatively soft malleable co-polymer. The most preferred polymer is a polymer alloy or melt blend including a polyamid or polycarbonate as the rigid polymer providing the strength and resistance to creep desired for this application. The relatively soft malleable co-polymer may be selected from various polymers including polyesters and polyolefins; however, a polymer alloy including a polycarbonate or polyamid and a polyester has been found particularly suitable for this application.

[0032] As will be understood, various polymeric melt blends, alloys, composites and co-polymers are being developed on a rapidly increasing basis and therefore the plastic collar of this invention is not limited to a specific polymer, provided the polymer has the desired physical properties described above. Suitable polymers for the plastic closures of this invention include EASTAR® MB polymers, which are melt blend and alloy polymers and EASTAR® thermoplastic polymers, which are neat polymers sold by Eastman Chemical Company of Kingsport, Tennessee and Eastman Chemical AG of Zug, Switzerland under the trade names "DA003, DN003" and "DN004". These materials are polymeric melt blends, alloys and co-polymers of polycarbonate or polyamid and polyester. As used herein, the terms melt blends and alloys refer to polymeric compositions having two or more polymers of different physical properties or characteristics, such as the EASTAR® polymers of Eastman Chemical Company

described above which include a polycarbonate or polyamid and a polyester. The polymer selected for the plastic collar of this invention may also include fillers and other constituents which would be more accurately described as a composite, although the base polymers may still be a polymeric melt blend or alloy. As used herein, the term alloy is used in its broadest sense to include alloys or melt blends, composites and co-polymers. As will be understood, the manufacturer or supplier of the raw material will normally blend the polymers based upon the specifications of the customer. The polymers may be co-injected to form a polymeric melt blend, alloy or composite or formed by any other suitable processes. It is anticipated, however, that other polymers having the described physical characteristics may also be utilized in the plastic collar or cap of this invention. In certain applications, it may also be desirable to coat at least the interior surface 43 of the collar shown in Figure 2 with a thermoplastic elastomer, or the entire collar may have a thin layer of a thermoplastic elastomer. The thermoplastic elastomer coating may be applied as a film or by co-injection with the polymer forming the collar 40. The closure 40 may be formed by injection molding.

[0033] Figures 4 to 6 and Figures 7 to 10 illustrate preferred alternative methods of crimping the closure or cap on a conventional cartridge, wherein the collar or cap 40 is gradually or incrementally deformed and rolled into the neck portion of the cartridge by cold forming. The embodiment of the crimping apparatus and method illustrated in Figures 4 to 6 may be utilized to seal cartridges or other containers with a plastic or elastomeric closure up to about 200 cartridges per minute. The crimping apparatus and method disclosed in Figures 7 to 10 may be used for higher volume applications, wherein the through put may be as great as 600 cartridges per minute.

[0034] In the embodiment of the crimping or capping apparatus disclosed in Figures 4 to 6, the crimping apparatus 100 includes a plurality of crimping tools, wherein the inclined surfaces of the crimping tools each have differing degrees of pitch, incrementally deforming

and rolling the free end 44 of the tubular portion 42 of the cap as now described. The embodiment of the crimping apparatus 100 shown in Figure 4 includes four rotatable crimping tools 102 to 108, each having a shaft 110 to 116, respectively, and an inclined or tapered surface 118 to 124, respectively, on the roller portion of the crimping tools 126 to 132, respectively. The pitch or angle of inclination of the inclined surfaces 118 to 124 decreases progressively as the cartridge progresses through the stations of the crimping apparatus. That is, the pitch of the inclined surface 120 of crimping tool 104 of the second station is less than the pitch of the inclined surface 118 of the crimping tool 102 of the first station, etc.

[0035] Figure 6 illustrates the first station of the crimping apparatus 100. The cartridge, stopper closure assembly 20 is supported on a support member 134, which is preferably resiliently biased to compress the radial portion 46 against the rim portion 36 of the elastomeric stopper 32 during crimping as set forth above. In the disclosed embodiment, the cartridge 22 is supported on a support member 134, which is supported on a base 136 by piston 140 and is spring biased by a suitable resilient member, such as spring 138. The upper or proximal end of the cartridge 22 and cap 40 is supported by a cup-shaped support member 142 which is affixed to rotatable shaft 144. The cup-shaped support member 142 may also be spring biased downwardly as shown by arrow 146. The assembly 20 is then rotated against the rotatable crimping tool 102 in the first station, which includes a rotatable shaft 110 having a roller portion 126. As set forth above, the roller portion 126 includes an inclined or tapered surface 118 which incrementally deforms the free end 44 of the tubular collar portion 42 radially inwardly into the reduced diameter neck portion 28 of the cartridge 22. The relative rotation of the crimping tool 102 and the cartridge assembly is shown by arrows 148 and 150, wherein the crimping tool and cartridge assembly are rotated at the same speed in opposite directions. As will be understood, however, one of the crimping tool and cartridge assembly

may be the drive member and the other may be the driven member wherein only the drive member is rotated and the other member follows. The base 136 is supported in the disclosed embodiment on a turntable 152, as shown in Figure 4, such that the cartridge assembly is moved from station to station. In the first station, as shown in Figure 6, the inclined surface 118 has a relatively steep angle, which deforms the free end 44 only partially into the reduced diameter neck portion 28 as shown at the right side of Figure 6. As set forth above, the inclined surface of the crimping tool at each station is reduced, such that the crimping tool in the final station 108 deforms the free end 44 of the tubular collar portion 42 into and against the reduced diameter neck portion and against the adjacent surface of the rim portion 26 of the cartridge barrel as shown in Figure 5. The crimping apparatus 100 thus performs the method of this invention as described above. That is, the free end 44 of the cap or closure 40 is incrementally deformed and rolled into the neck portion 28 by the plurality of crimping tools avoiding stress cracking and discoloration of the clear polymeric cap.

[0036] Figures 7 to 10 illustrate a preferred alternative crimping apparatus 200, wherein the crimping tool includes a circular rail 202 supported on a suitable support 204. The rail 202 includes an inclined surface 206 which gradually and continuously changes in pitch from the inlet 208 to the outlet 210. That is, the tubular collar portion 204 is driven against the tapered surface 206 at the inlet 208 and the pitch of the tapered surface is continuously decreased along the rail to the outlet 210. The cartridge assembly 320 illustrated in Figures 7 to 10 and best shown in Figure 10 includes a cartridge or cartridge barrel 322 having an open end 324, a radial rim portion 326 adjacent to but spaced from the open end 324 and a reduced diameter neck portion 328. The container portion 330 in this embodiment includes an enlarged bypass portion 324, the purpose of which is described below. The proximal open end 324 of the cartridge includes a cup-shaped stopper 332 including a tubular rim portion 336 and a central portion 338. As shown in Figures 7 to 10, the rim portion 336 of the cup-

shaped stopper engages the rim portion 326 of the cartridge barrel. The closure of cap 340 is similar to the cap 40 described above in regard to Figures 1 to 3, except that the tubular portion 342 is essentially perpendicular to the radial portion 346 to accommodate the cup-shaped stopper 332. The closure 340 includes a central opening 348 and the tubular collar portion 342 includes a free end 344 surrounding the reduced diameter neck portion 328 as best shown in Figures 8 to 10.

[0037] The distal open end 352 of the cartridge barrel includes a second stopper 350 as described above. In this embodiment, however, the cartridge assembly includes a third stopper 354 spaced from the second stopper 350 adjacent the bypass 324. Thus, the cartridge assembly 320 best shown in Figure 10 may include a combination of medicaments, drugs or vaccines or a liquid 355, such as a diluent and a dry or powdered medicament, drug or vaccine 356. Thus, as the second stopper 350 is driven through the cartridge barrel 322 against the liquid 355, the third stopper 354 is driven into the enlarged bypass 324 and the liquid 355 flows around the stopper 354 through the bypass 324 into the powder 356. Where the liquid 355 is a diluent and the substance 356 is a dry or lyophilized medicament, drug or vaccine, the diluent 355 will flow through the bypass 324 and reconstitute the dry or powdered drug, vaccine or medicament 356.

[0038] With the crimping apparatus 200 illustrated in Figures 7 to 10, the cartridge assembly 320 is continuously rotated as the tubular collar portion is driven against the rail as shown by arrows 212 and 214. Figure 8, which is a partial cross sectional view through view arrows 8-8, illustrates the initial deformation of the free end 344 tubular collar portion 342 adjacent the entrance 208, wherein the angle of inclination of the chamfered or frustoconical surface 206 is relatively steep, such as about 40 to 50 degrees or greater. Figure 9, which is a partial cross sectional view through view arrows 9-9, illustrates the angle of inclination of the chamfered surface 206 of the rail 204 about midway through the cold deformation and rolling

of the tubular collar portion, wherein the angle of inclination is less than 40 degrees. Finally, Figure 10 illustrates the angle of inclination 206 of the chamfered surface adjacent the outlet 210, wherein the angle of inclination is less than 30 degrees, fully deforming the free end 344 of the tubular collar portion 342 into the reduced diameter neck portion 328 of the cartridge and against the rim portion 326. Thus, the rim portion is gradually or incrementally deformed and rolled by the continuously decreasing angle of inclination of the chamfered or frustoconical surface 206 in a gradual and continuous process. Figure 10 also illustrates the simultaneous compression of the radial portion 346 of the collar against the rim portion 336 of the stopper during cold forming of the tubular collar portion 344 as described above in regard to Figure 6, which is a preferred embodiment of the method of this invention.

[0039] Thus, in both of the preferred embodiments of the disclosed apparatus for cold forming the free end of the plastic closure into the reduced diameter neck portion of the cartridge or other medical container as described above and shown in Figures 4 to 6 and Figures 7 to 10, respectively, the free end is gradually or incrementally deformed radially and rolled into the neck portion to assure permanent deformation, reduce creep which could result in leakage and reduce damage to the closure, such as cracking or discoloration of a clear plastic closure. Thus, the method of this invention provides a simple and relatively inexpensive method of crimping or cold forming a plastic closure or collar which avoids the disadvantages of a malleable metal closure or collar and which assures complete sealing of the cartridge without damage to the polymeric closure and rim portion of the cartridge. The tubular collar portion of the closure or collar may also be deformed into the reduced diameter neck portion of the cartridge or other container by a crimping device (not shown) having a jaw which deforms the free end portion of the tubular collar portion into the neck portion one at a time provided the deformation is gradual to avoid damage to the collar portion.

[0040] Figure 11 illustrates an alternative embodiment of a cartridge assembly 420 sealed with a polymeric cap or closure by the method of this invention. The cartridge or cartridge barrel 422 may be formed of glass as described above and includes an open proximal end 424, a radial rim portion 426 surrounding the open end, a reduced diameter neck portion 428 adjacent the neck portion and a container portion 422. An elastomeric stopper 432 is received over the open end having a rim portion 436 received on the rim portion 426 of the cartridge barrel and a center portion 438 bridging the open end. The cap or closure 440 includes a tubular collar portion 422 having a free end 444 which is incrementally deformed and rolled into the reduced diameter neck portion 428 by the method of this invention as described and the cap or closure 440 further includes an integral radial portion 446 received over the rim portion 436 of the stopper and the rim portion 426 of the cartridge barrel. The stopper includes a central opening 448 to receive a needle cannula (not shown) for dispensing the medicament, drug or vaccine contained in the container portion 430 as described below.

[0041] In this embodiment of the cartridge assembly 420, the cartridge includes a second stopper 450 received in the open distal end 452 as described above and a third stopper 354 received in an integral radial bridging portion 356 separating the container portion 430 into two compartments 370 and 372 separated by the third stopper 354. The radial deformation of the free end 444 of the cap or stopper 440 is schematically illustrated in Figure 11 similar to Figure 3. That is, the free end 444 of the closure 440 is incrementally deformed and rolled into the reduced diameter neck portion 428 of the cartridge barrel 422 by a crimping tool shown schematically at 458 having an inclined surface 460. The crimping tool is rotated on a shaft 462 as shown by an arrow 464. As will be understood, however, from the description of the preferred crimping apparatus disclosed in Figures 4 to 6 and 7 to 10 above, the free end 444 of the tubular collar portion 442 is incrementally crimped and rolled into the reduced

diameter neck portion 428 of the cartridge barrel either by a plurality of crimping tools having decreasing angles of inclination as disclosed in Figures 4 to 6 or a continuous rail having a continuously decreasing angle of inclination as disclosed in Figures 7 to 10 thereby avoiding stress cracking or discoloration of the clear polymeric cap or closure 440. The operation of the cartridge assembly 420 shown in Figure 11 is similar to the cartridge assembly 320 shown in Figure 10, wherein the second stopper 450 is driven into the first container portion 370 against the liquid contained in this compartment, which drives the third stopper 354 through the opening in the bridge portion 356, intermixing the substances in these compartments which is then dispensed by a needle cannula (not shown) which pierces the central portion 438 of the stopper 432 in a medicament delivery pen such as disclosed in the above referenced U.S. Patent No. 5,549,575.

[0042] The deformation of the free end of the collar portion in each of these embodiments is a cold forming process which, as set forth above, also relies upon the polymer selected for the collar or closure. That is, the polymer selected must be sufficiently malleable to permit radial deformation or crimping without forming stress cracking or fractures. Further, the polymer must be sufficiently rigid to retain its shape following deformation. Finally, the polymer must also be sufficiently resistant to creep to maintain the seal between the plastic closure or collar and the container following radial deformation to prevent leakage or contamination of the materials stored in the container. One important advantage of the method of this invention is that the crimping process may be performed in an aseptic environment preventing contamination of the material within the cartridge and the assembly. As set forth above, another important advantage of the method of this invention is that the improved polymeric closure eliminates the potential contamination and hazards associated with malleable metal closures, such as aluminum. As will be understood, various

modifications to the disclosed methods of sealing a cartridge or other container with a polymeric closure of this invention within the purview of the appended claims.